PSJ2 Exh 48

Pain Management

May 5, 2009

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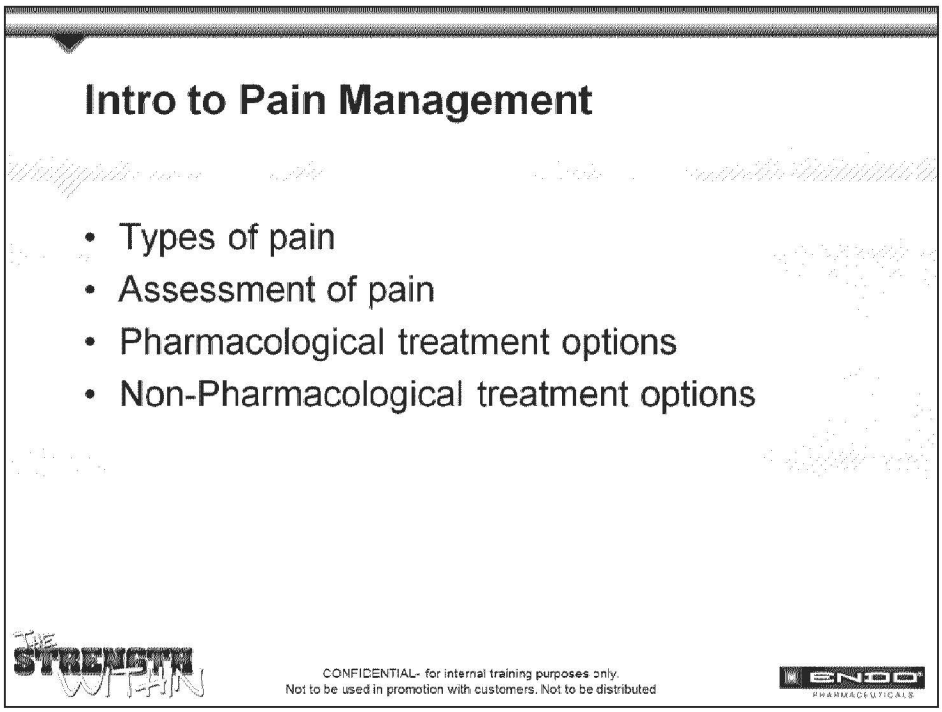
President Maryland Pain Society


Intro to Pain Management
• Types of pain
• Assessment of pain
• Pharmacological treatment options
• Non-Pharmacological treatment options
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Epidemiology of Pain

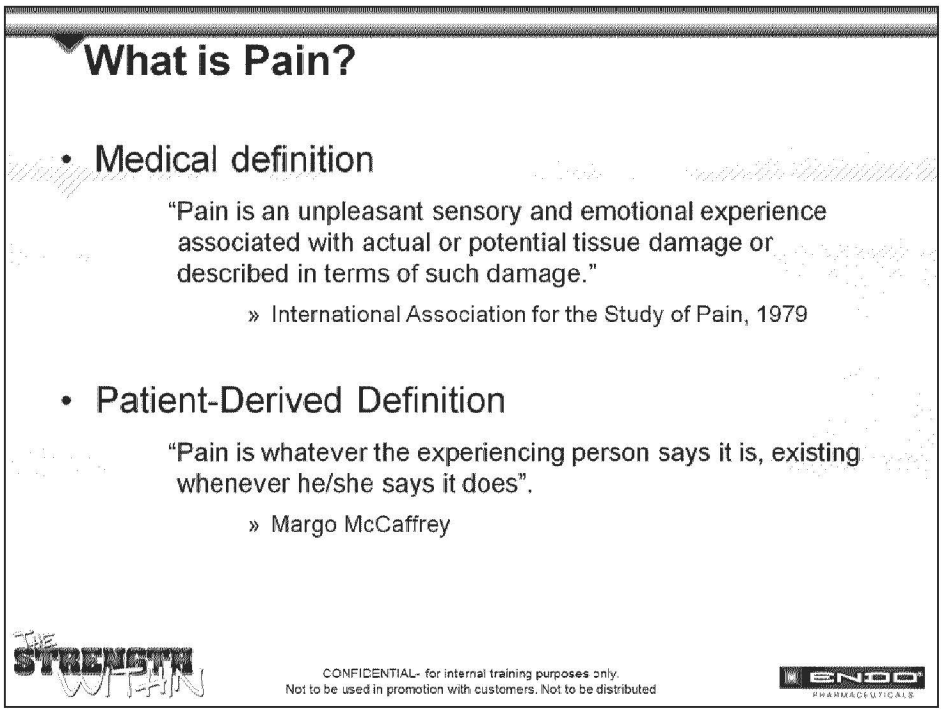
- An estimated 76.5 million Americans (26%) aged 20 years and over report that they have had a problem with pain of any sort that persisted for more than 24 hours in duration (not including acute pain)
- 20% of American adults (42 million people) report that pain or physical discomfort disrupts their sleep a few nights a week or more
- Chronic pain disables more people than cancer or heart disease and costs the American people more than both combined
- The annual cost of chronic pain in the US, including healthcare expenses, lost income, and lost productivity is estimated to be $100 billion

Source: APF; Decision Resources- Chronic Pain, March 2008; National Center for Health Statistics Report: Health, US, 2006, Special Feature on Pain

Epidemiology of Pain

Disease Population in the US	% Diagnosed	% Drug Treated
Osteoarthritis pain	53	50
Rheumatoid arthritis pain	98	95
Cancer pain		
Severe	85	75
Bone	75	75
Neuropathic	70	60
Breakthrough	80	75
Chronic low back pain	65	80
Fibromyalgia	22	85
HIV-related neuropathic pain	38	53

Source: APF: Decision Resources- Chronic Pain, March 2008; National Center for Health Statistics Report: Health, US, 2006, Special Feature on Pain


What is Pain?
• Medical definition
"Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage."
» International Association for the Study of Pain, 1979
• Patient-Derived Definition
"Pain is whatever the experiencing person says it is, existing whenever he/she says it does".
» Margo McCaffrey
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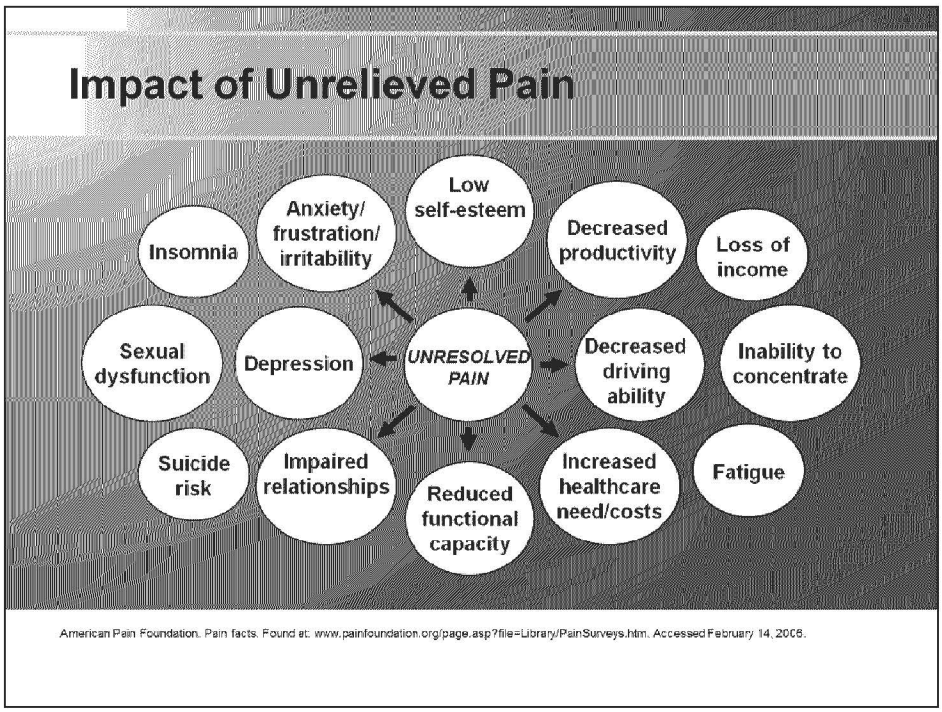


Unresolved chronic pain has a negative impact on the sufferers' quality of life, affecting ability to concentrate, do their job, exercise, socialize, get a good night's sleep, perform household chores, and have sex. It affects their participation in activities, results in missed work, and is associated with fatigue, frustration, anxiety, irritability, and depression. Pain interferes with their ability to sleep, productivity, and ability to work. Some feel they cannot function as normal people and feel so bad they want to die.

Reference

American Pain Foundation. Pain facts. Found at: www.painfoundation.org/page.asp?file=Library/PainSurveys.htm. Accessed on October 19, 2006.

Disability

- 86 million Americans suffer from chronic pain
- Low Back Pain
  - Leading cause of disability in adults <45
  - 3rd leading cause of disability in adults >45
  - Nearly 8 million people in US partially disabled due to LBP

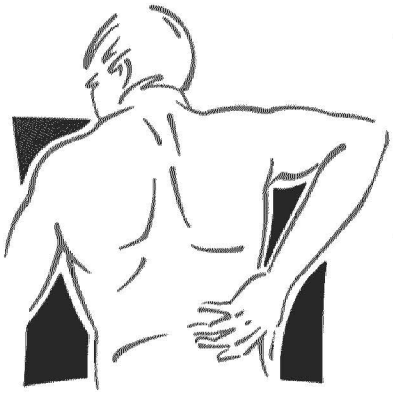
Sources:
http://www.theacpa.org/nerve/about_acpa.asp
http://emedicine.medscape.com/article/310353-overview
http://www.karger.com/gazette/65/walsh/art_4_p.htm

THE STRENGTH WITHIN

ENDO PHARMACEUTICALS

Return to Work

- Less than 50% if off work for greater than 6 months
- 25% will return if > 1 year
- Nearly 0% if > 2 years



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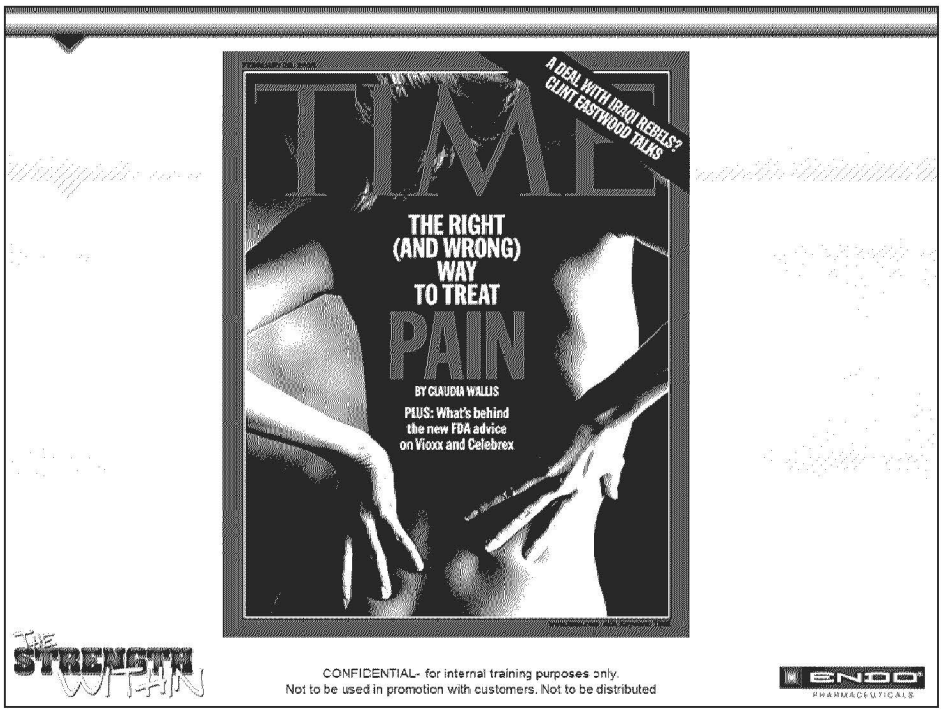
TIME
A DEAL WITH IRAQI REBELS? CLINT EASTWOOD TALKS
THE RIGHT (AND WRONG) WAY TO TREAT
PAIN
BY CLAUDIA WALLIS
PLUS: What's behind the new FDA advice on Vioxx and Celebrex
THE STRENGTH WITHIN
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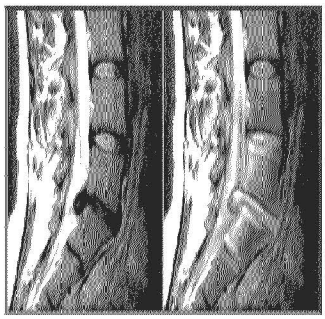
Pain Assessment

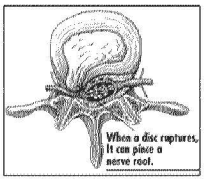
- Character
- Onset
- Location
- Duration
- Intensity
- Alleviating factors
- Exacerbating factors

Herniated Disc



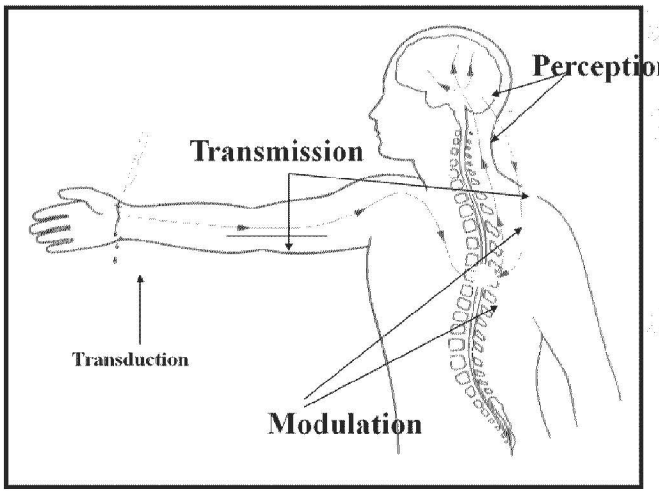
HNP/bulge on MRI

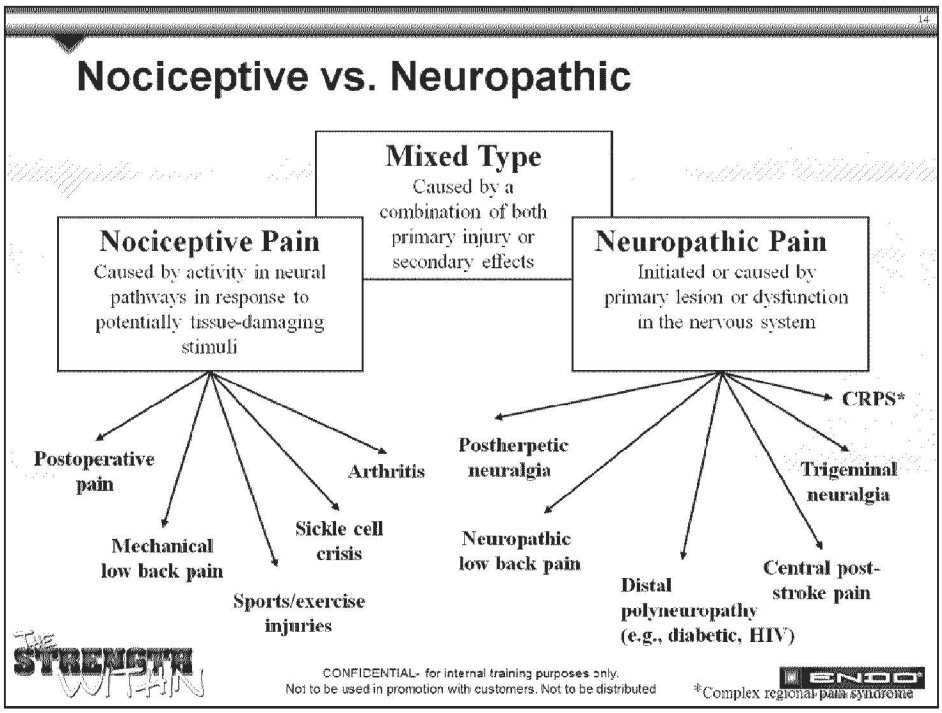
- Jensen found 64% of adults without back pain had a bulge, protrusion, or extrusion at one level
- 38% had abnormality at more than one level



Jensen MC et al. Magnetic resonance imaging of the lumbar spine in people without back pain. N Engl J Med 1994;331:69-73

Basic Process of Normal Pain Processing





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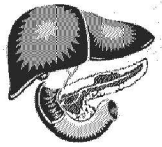
Galer BS, Dworkin RH. *A Clinical Guide to Neuropathic Pain*. Minneapolis, Minn: The McGraw-Hill Companies Inc; 2000:8-9.

15

Nociceptive Pain
Somatic vs. Visceral

- Somatic
  - Deep or cutaneous tissue injury; localized
  - Described as dully, achy, gnawing
  - Responsive to opioids & NSAIDs
  - Examples
    - Tumor, bone mets, fractures, muscle pulls

- Visceral
  - Organ system origin; poorly localized
  - Described as diffuse and achy
  - Responsive to opioids
  - Examples
    - Tumor infiltrate, bowel obstruction, pancreatic CA



Neuropathic Pain

- Results from damage to or changes of peripheral or central nervous system
- Often described as burning, sharp, electrical, lightning symptoms

•Peripheral Neuropathies

– Diabetic, Alcohol.

•Entrapment Neuropathies

– CTS, Neuromas

•CRPS

- RSD

•Central Pain

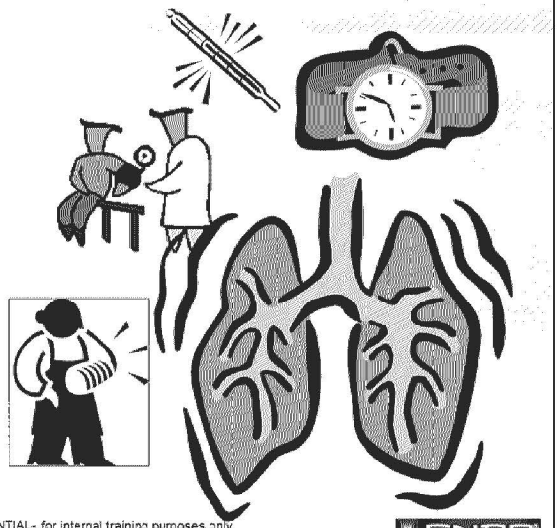
- Post CVA Pain, MS

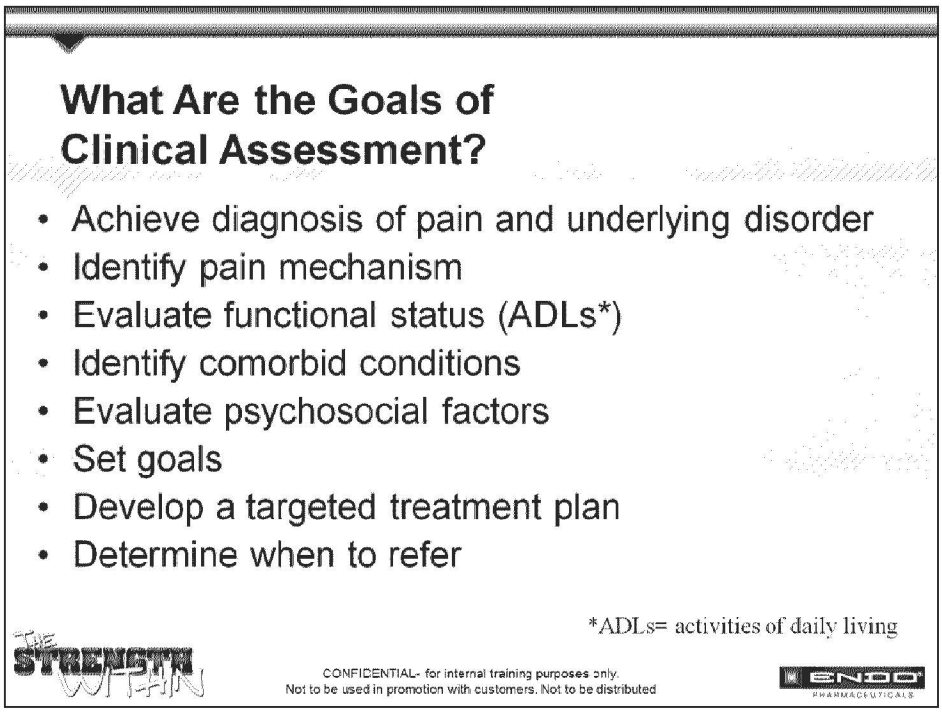
17

Pain Assessment

5th Vital Sign

1. Temperature
2. Pulse
3. Respiration rate
4. Blood pressure
5. PAIN




What Are the Goals of Clinical Assessment?
• Achieve diagnosis of pain and underlying disorder
• Identify pain mechanism
• Evaluate functional status (ADLs*)
• Identify comorbid conditions
• Evaluate psychosocial factors
• Set goals
• Develop a targeted treatment plan
• Determine when to refer
*ADLs= activities of daily living
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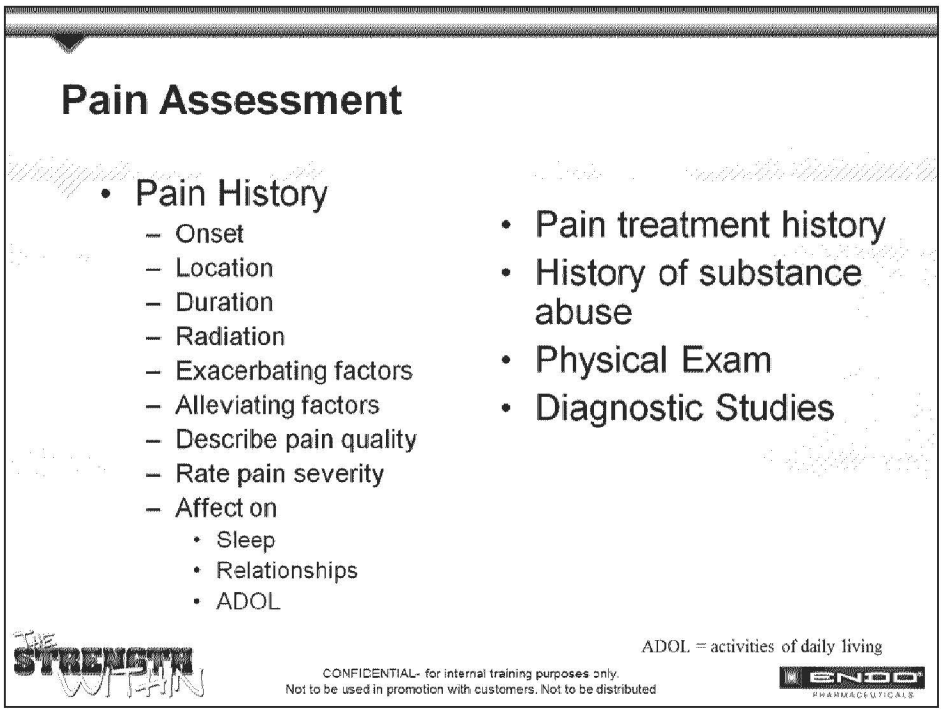
Pain Assessment
• Pain History
– Onset
– Location
– Duration
– Radiation
– Exacerbating factors
– Alleviating factors
– Describe pain quality
– Rate pain severity
– Affect on
• Sleep
• Relationships
• ADOL
• Pain treatment history
• History of substance abuse
• Physical Exam
• Diagnostic Studies
ADOL = activities of daily living
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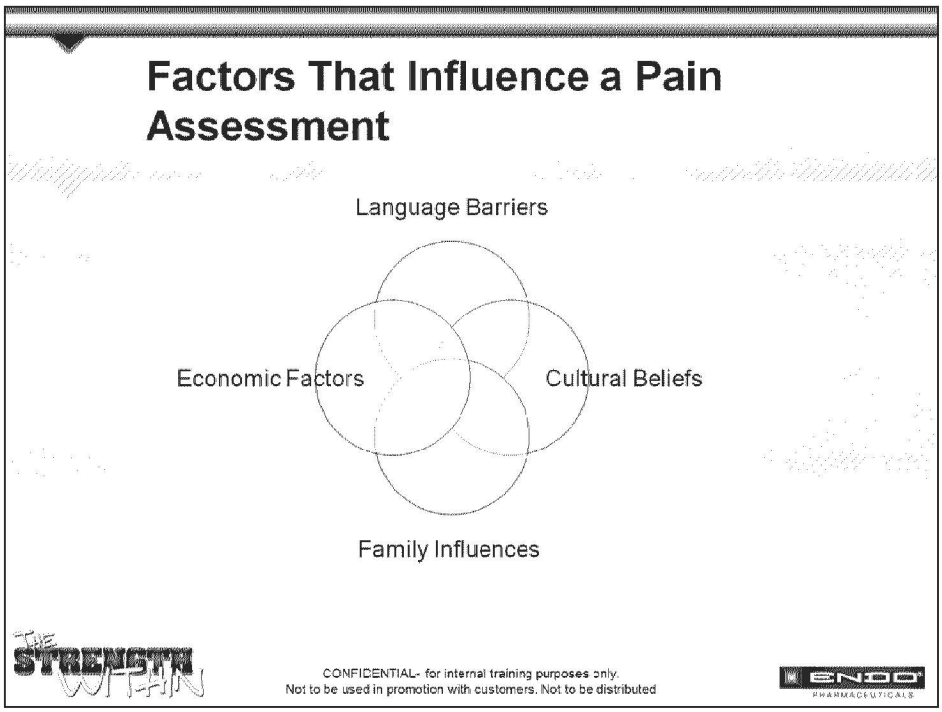
Factors That Influence a Pain Assessment
Language Barriers
Economic Factors
Cultural Beliefs
Family Influences
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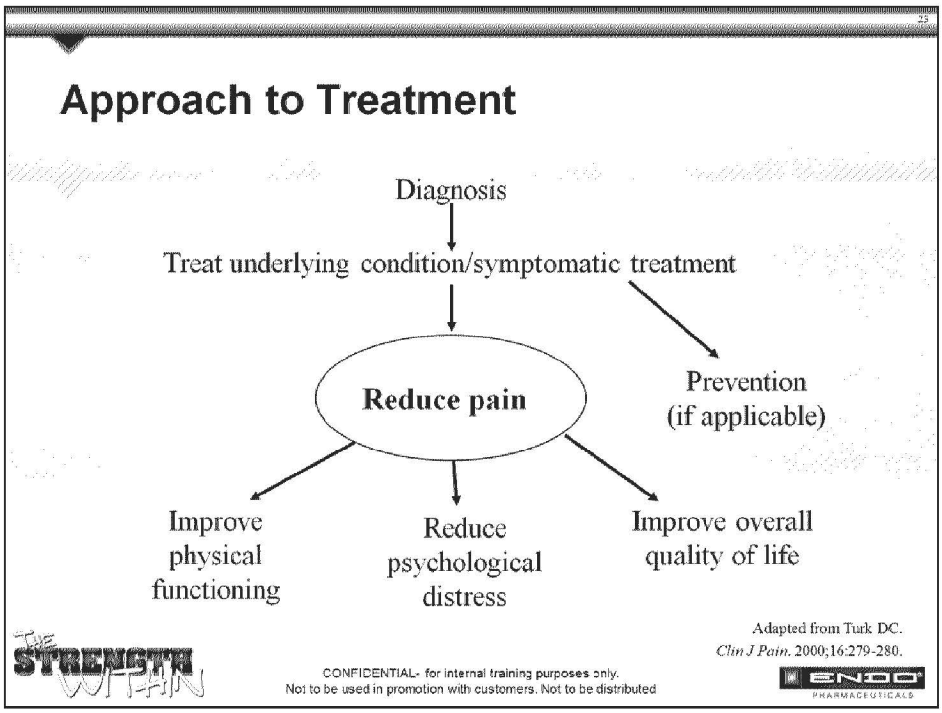
Pain Measurement Tools

- Pain Diary
- Visual Analog Scale (VAS)
- Verbal Numerical Scale
- Wisconsin Brief Pain Inventory (BPI)
- McGill Pain Questionnaire
- WOMAC Osteoarthritis Index
- Neuropathic Pain Scale (NPS)



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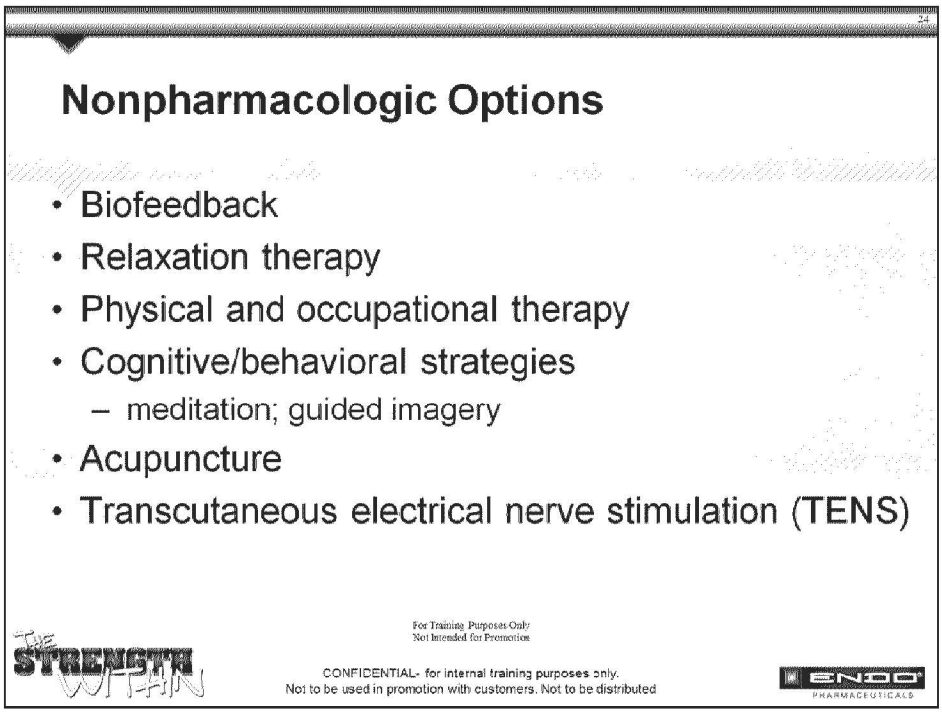

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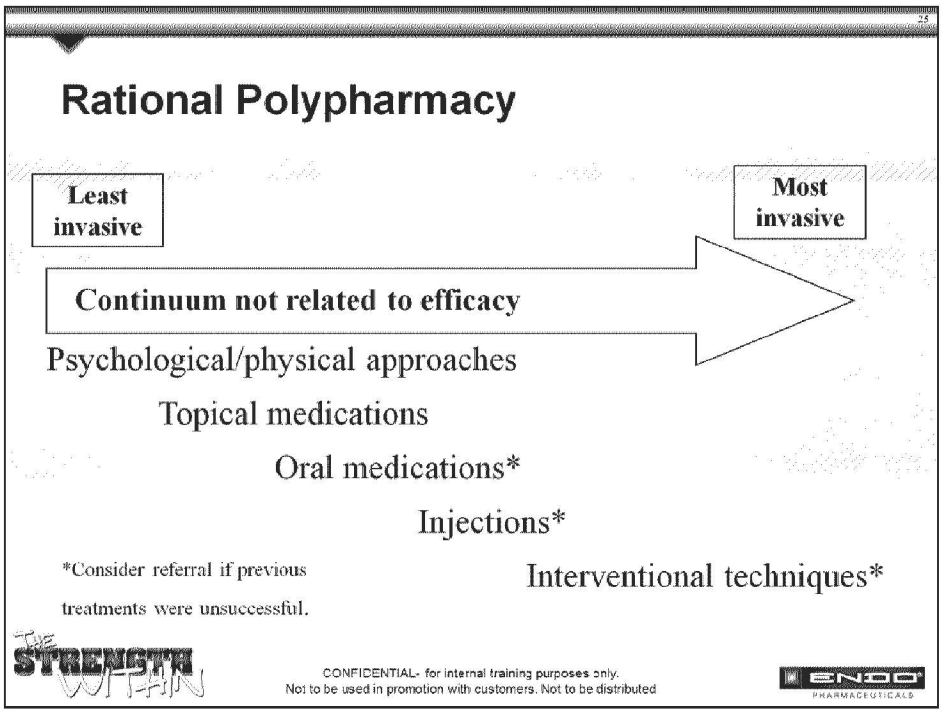
Kuman D, Marshall HJ. Diabetic peripheral neuropathy: amelioration of pain with transcutaneous electrostimulation. *Diabetes Care*. 1997;20:1702-1705.



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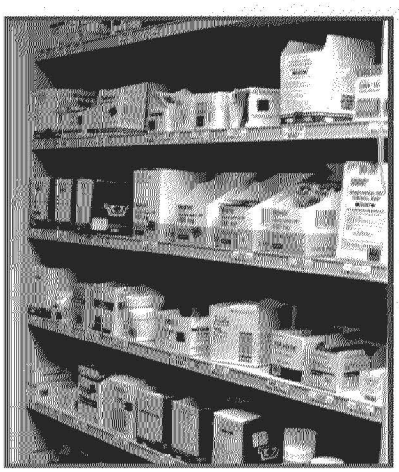
2. Katz N. *Clin J Pain*. 2000;16:S41-S48.
3. Leland JY. *Geriatrics*. 1999;54:23-37.
4. Belgrade MJ. *Postgrad Med*. 1999;106:127-140.
5. Galer BS et al. *A Clinical Guide to Neuropathic Pain*. 2000:97.
6. Gonzales GR. *Neurology*. 1995;45(suppl 9):S11-S16.

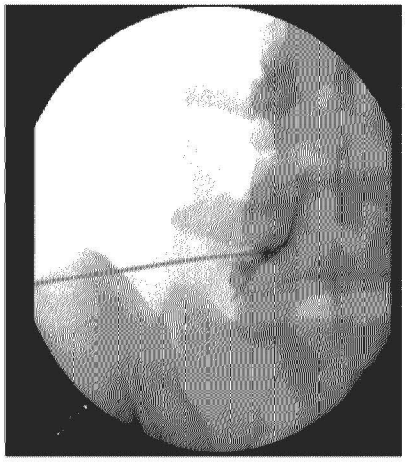
Medication Management

- Reversible, titratable
- Adjuvant meds treat concurrent symptoms
- Use of multiple drugs is typical in chronic pain mgmt
- Lack of invasiveness



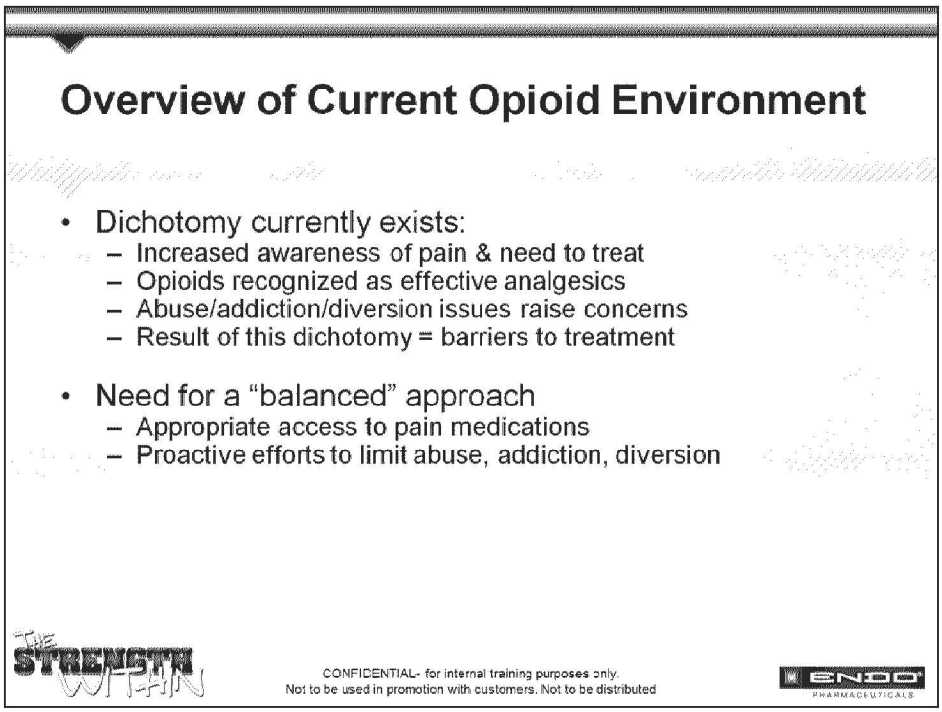
Limitations of Pharmacotherapy

- Abuse, diversion
- Compliance
- Side effects
- If pain is localized to one region, is there a targeted treatment (e.g. injection, surgery)?



Opioid Treatment of Acute and Chronic Pain

- Use of analgesics should include
  Proper patient selection
  1. A proper initial assessment of the patient
  2. The use of opioids as part of a comprehensive treatment plan e.g., consider non-opioid treatments as well
  3. Patient reassessment- analgesia? Adverse effects? Activities of daily living? Aberrant behaviors?
  4. Opioid rotation- rotation from one opioid to another can result in significant improvement in analgesia


Overview of Current Opioid Environment
• Dichotomy currently exists:
– Increased awareness of pain & need to treat
– Opioids recognized as effective analgesics
– Abuse/addiction/diversion issues raise concerns
– Result of this dichotomy = barriers to treatment
• Need for a "balanced" approach
– Appropriate access to pain medications
– Proactive efforts to limit abuse, addiction, diversion
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Opioid Basics

- No ceiling dose
- No End Organ Toxicity
- Opioid tolerance will develop!!!!
- Opioid dependence may develop.
- Opioid addiction unlikely to develop.
  - –If pain exists then addiction = 1: 10,000

Controlled Substance Act

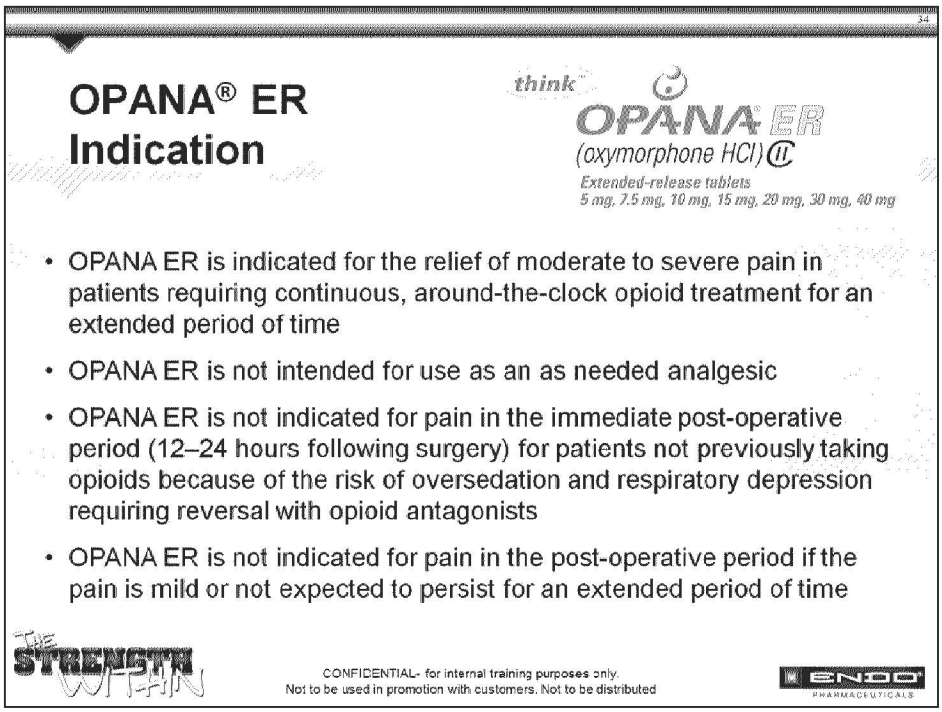
- Scheduling due to medical use & potential for abuse
- Five schedules: C-I, C-II, C-III, C-IV, C-V
- C-I: No accepted medical use (i.e., LSD)
- C-II: Accepted med. use; high abuse potential
  - i.e., Morphine, hydromorphone, oxymorphone
- C-III: "Less" abuse vs. C-1or C-2
  - i.e., Hydrocodone w/APAP

APAP=Acetaminophen

Definition Related to Opioid Use

- Physical Dependence
  - Defined solely by the occurrence of an abstinence syndrome on abrupt does reduction or discontinuation.
- Tolerance
  - Diminution of one or more drug effects cause by exposure of drug
- Addiction
  - Aberrant use of substance characterized by lose of control, compulsive use, and continue use despite harm to self

	OPANA ER	OxyContin	Avinza	Kadian
Active Compound	Oxymorphone	Oxycodone	Morphine	Morphine
Dosing	Pivotal trials demonstrate proven every 12 hour dosing that is maintained over 12 week period	Every 12 hours	Once-a-day	Once or twice-a-day
Half-life	IR = up to 9 hours ER = up to 11.3 hours	IR = 3.2 hours CR = 4.5 hours	Not listed	Not listed
Metabolism	Metabolized in the liver. No CYP450 drug/drug interactions at clinically relevant doses. No dose adjustment necessary for CYP3A4 or CYP 2C9-mediated interactions	CYP450 2D6	Conjugated in the liver	Conjugated in the liver
Relative Potency	10 mg	20 mg	30 mg	30 mg
Delivery System	TIMERx-N matrix	AcroContin - biphasic	Encapsulated beads	Encapsulated pellets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OPANA® ER
Indication
think
OPANA ER
(oxymorphone HCl)
Extended-release tablets
5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg
• OPANA ER is indicated for the relief of moderate to severe pain in patients requiring continuous, around-the-clock opioid treatment for an extended period of time
• OPANA ER is not intended for use as an as needed analgesic
• OPANA ER is not indicated for pain in the immediate post-operative period (12–24 hours following surgery) for patients not previously taking opioids because of the risk of oversedation and respiratory depression requiring reversal with opioid antagonists
• OPANA ER is not indicated for pain in the post-operative period if the pain is mild or not expected to persist for an extended period of time
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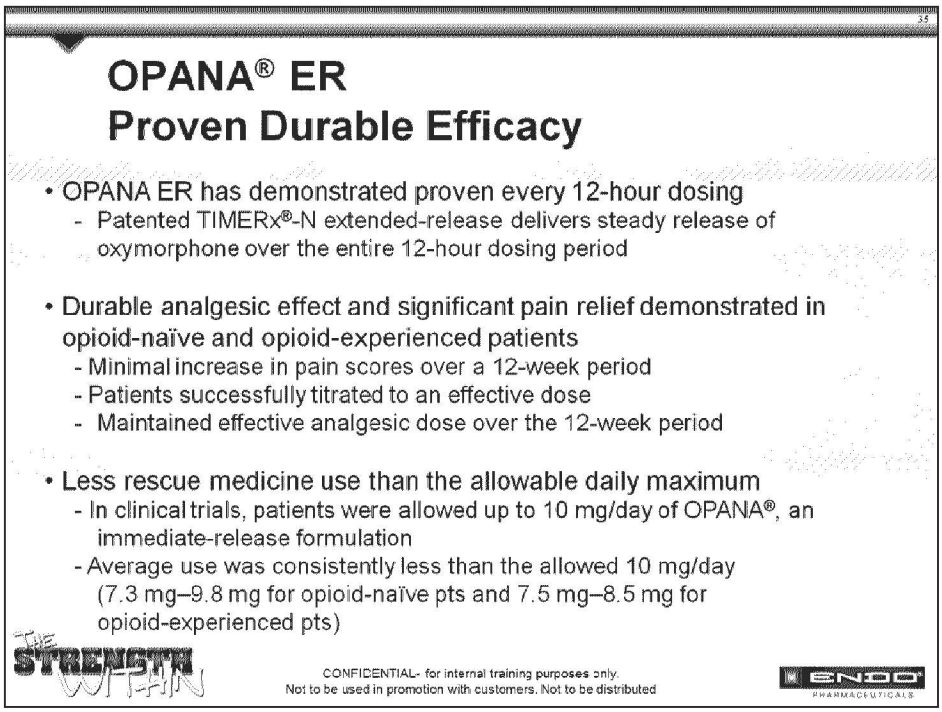
OPANA® ER
Proven Durable Efficacy
• OPANA ER has demonstrated proven every 12-hour dosing
- Patented TIMERx®-N extended-release delivers steady release of oxymorphone over the entire 12-hour dosing period
• Durable analgesic effect and significant pain relief demonstrated in opioid-naïve and opioid-experienced patients
- Minimal increase in pain scores over a 12-week period
- Patients successfully titrated to an effective dose
- Maintained effective analgesic dose over the 12-week period
• Less rescue medicine use than the allowable daily maximum
- In clinical trials, patients were allowed up to 10 mg/day of OPANA®, an immediate-release formulation
- Average use was consistently less than the allowed 10 mg/day (7.3 mg–9.8 mg for opioid-naïve pts and 7.5 mg–8.5 mg for opioid-experienced pts)
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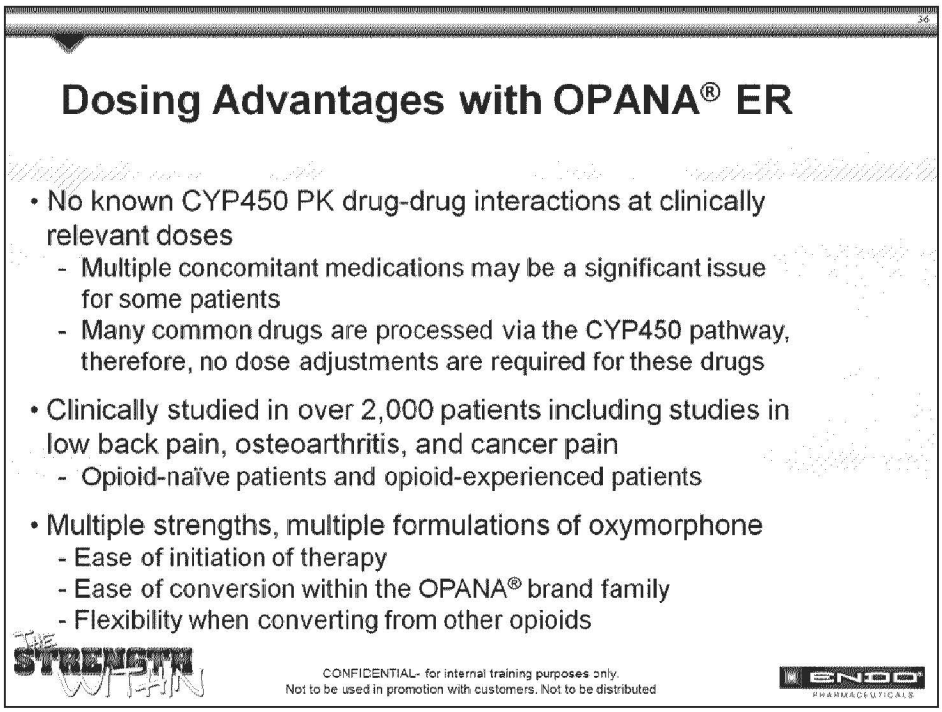
Dosing Advantages with OPANA® ER
• No known CYP450 PK drug-drug interactions at clinically relevant doses
- Multiple concomitant medications may be a significant issue for some patients
- Many common drugs are processed via the CYP450 pathway, therefore, no dose adjustments are required for these drugs
• Clinically studied in over 2,000 patients including studies in low back pain, osteoarthritis, and cancer pain
- Opioid-naïve patients and opioid-experienced patients
• Multiple strengths, multiple formulations of oxymorphone
- Ease of initiation of therapy
- Ease of conversion within the OPANA® brand family
- Flexibility when converting from other opioids
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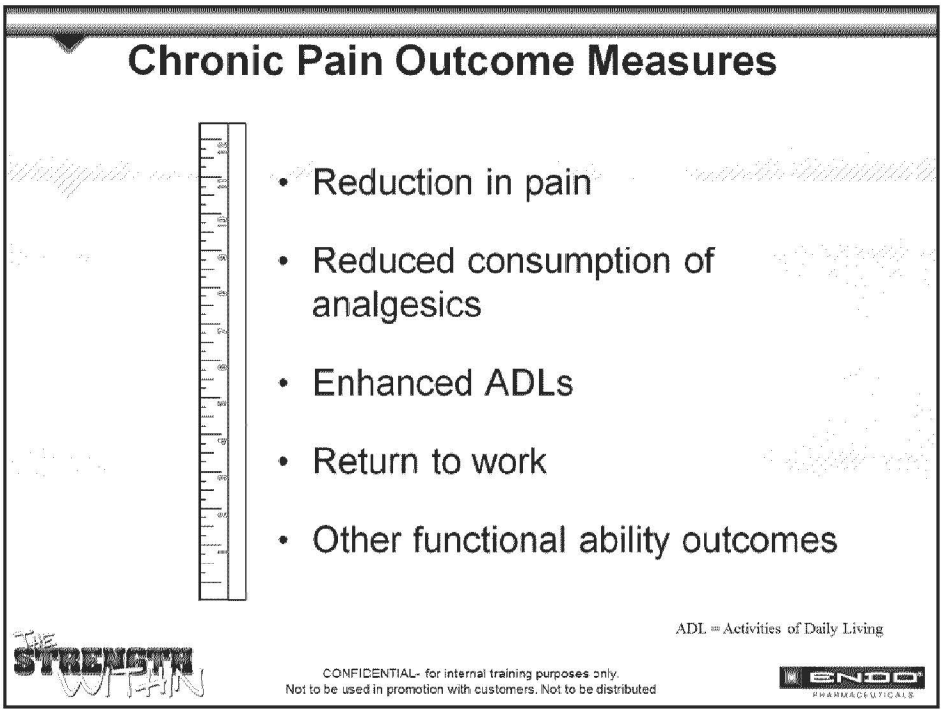

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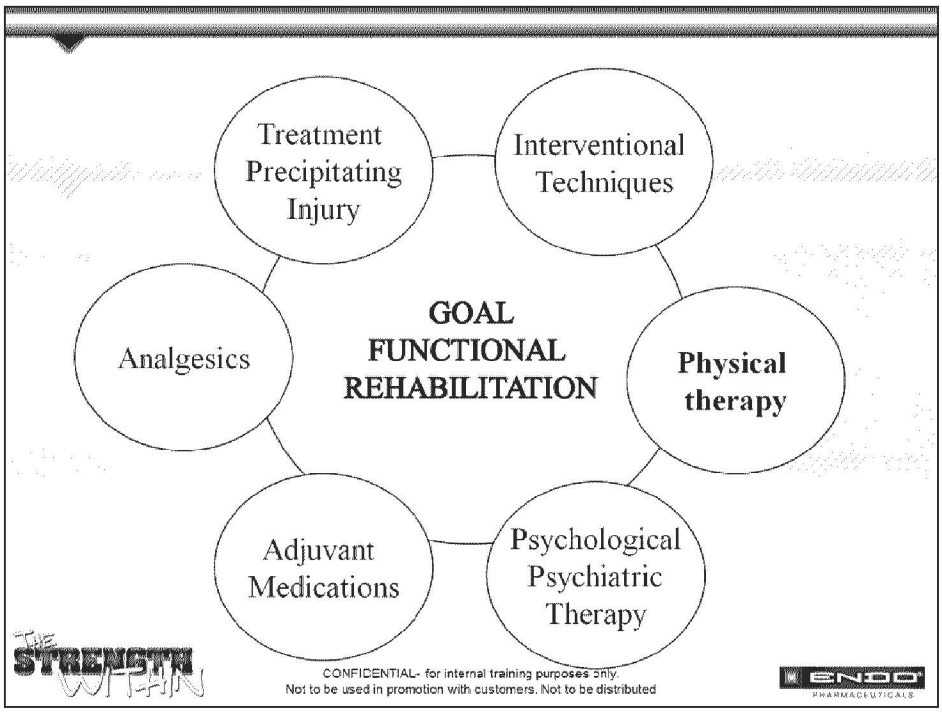
• The outcome measures I have used to organize the results reported in the literature are reduction in pain, discontinued or greatly reduced consumption of oral analgesics, enhanced performance of activities of daily living, return to work and other functional ability outcomes.


Treatment Precipitating Injury
Interventional Techniques
Analgesics
GOAL
FUNCTIONAL
REHABILITATION
Physical therapy
Adjuvant Medications
Psychological Psychiatric Therapy
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